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UNITED STATES DISTRICT COURT
DISTRICT OF UTAH

NUTRACEUTICAL CORPORATION and)	
SOLARAY, INC.,)	
)	
Plaintiffs,)	
)	
v.)	Case No. 2:04CV00409 PGC
)	
ANDREW VON ESCHENBACH, M.D.,)	
Commissioner, U.S. Food and Drug)	
Administration, <u>et al.</u> ,)	
)	
Defendants.)	

DEFENDANTS' REPLY TO PLAINTIFFS' OPPOSITION TO
DEFENDANTS' CROSS-MOTION FOR SUMMARY JUDGMENT

INTRODUCTION

As Defendants established in their cross-motion for summary judgment, Nutraceutical's challenges to the validity of FDA's regulation (Final Rule)¹ lack merit. First, FDA gave proper notice and opportunity for comment on the agency's plan to rely on the unreasonable risk standard – which unambiguously requires a risk-benefit analysis – to determine whether dietary supplements containing ephedrine alkaloids (EDS) are adulterated. Second, FDA's decision not to include conventional foods containing ephedrine alkaloids in the Final Rule's ban of EDS was not arbitrary and capricious because the unreasonable risk standard applies only to dietary supplements and cannot be used to find conventional foods adulterated.

Nothing in Nutraceutical's opposition refutes these points. In its opposition, Nutraceutical distorts the requirements of the APA and the language of the 1997 Proposed Rule in an unavailing attempt to create an additional notice and comment obligation that did not exist. Additionally, Nutraceutical's argument that FDA acted arbitrarily and capriciously in treating dietary supplements differently from conventional foods ignores the relevant statutory scheme. In sum, Nutraceutical's legal arguments are meritless.

Further, Nutraceutical's extensive factual discussion is largely beside the point, and nothing in this section of Nutraceutical's opposition creates a genuine issue of material fact.²

¹ Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk, 69 Fed. Reg. 6788 (Feb. 11, 2004), codified at 21 C.F.R. § 119.1.

² It is worth nothing that, although immaterial, Nutraceutical's allegation that the product label, which is filed as Exhibit A to its summary judgment motion, is the same product label contained in the administrative record, which was filed with the agency as part of the company's April 7, 2003, comments, is wrong. See Pls. Opp. at x-xi; compare Pls. Exh. A (label bears no statement disclosing the percentage of ephedrine alkaloids per capsule, copyright date "MMIII")

Indeed, many of the facts that Nutraceutical emphasizes in the fact section relate only to issues already decided by the Tenth Circuit in its decision in this case. Accordingly, the government is entitled to summary judgment as a matter of law.

ARGUMENT

I. THE FINAL RULE COMPLIES WITH THE APA'S NOTICE AND COMMENT PROCEDURES

Nutraceutical's argument that FDA did not comply with the notice and comment requirements of the APA has shifted focus yet again. See Defs. Mem. at 9-10 (explaining Nutraceutical's first "adjustment"). Nutraceutical now asserts that FDA did not give the public adequate notice and opportunity for comment on the unreasonable risk standard because the statutory language is "not self-executing" and therefore "[e]ach term, 'risk,' 'benefit,' and 'comparison'" must be further interpreted and "assigned weights before a 'test' using those terms can be applied." Pls. Opp. at 2. This argument distorts APA requirements.

Nothing in the APA required FDA to conduct a separate notice-and-comment proceeding on its interpretation of "unreasonable risk" or "risk-benefit analysis" before applying the unreasonable risk standard in 21 U.S.C. § 342(f)(1)(A) to EDS through rulemaking. The Tenth Circuit held, "Congress unambiguously required the FDA to conduct a risk-benefit analysis under DSHEA [Dietary Supplement Health and Education Act]" to determine whether EDS pose an unreasonable risk of illness or injury. Nutraceutical v. von Eschenbach, 459 F.3d 1033, 1038 (10th Cir. 2006). FDA's application of the risk-benefit requirement to EDS did not involve a "legislative function" (Pls. Opp. at 10), but rather involved the kind of medical and scientific

with Pls. Exh. C, attachment to April 7, 2003, comments (label bears statement disclosing the percentage of ephedrine alkaloids per capsule, copyright date "MMII").

judgments that the agency scientists are best able to make. The concept is not unique – risk-benefit analyses are required by other provisions of the Federal Food, Drug, and Cosmetic Act (FDCA) and by other public health statutes, as well as in other legal contexts. See, e.g., Nutraceutical, 459 F.3d at 1038 (describing another FDCA provision that involves a comparison of risks and benefits); see also id. at 1040. The Final Rule meets the APA's notice and comment requirements because FDA gave the public fair notice and opportunity for comment on the fact that the agency was contemplating whether to declare EDS adulterated under the unreasonable risk standard, § 342(f)(1)(A).³

Congress authorized FDA to determine whether EDS present an "unreasonable risk of illness or injury" under § 342(f)(1)(A). During the EDS rulemaking, the public had several opportunities to comment on FDA's proposed regulatory options and on the wealth of scientific information in the public docket that was relevant to whether EDS present an unreasonable risk – i.e., the pharmacology of ephedrine alkaloids, peer-reviewed scientific literature on the effects of ephedrine alkaloids, adverse event reports of individuals following consumption of EDS, and

³ According to Nutraceutical, FDA believes that the rule is not substantive. Pls. Opp. at 3 n.10. This is not the case. Indeed, FDA explicitly stated that the Final Rule is a substantive rule. See Defs. Mem. at 16 ("The only substantive rule at issue here is the Final Rule, which concluded that EDS are adulterated and, therefore, can no longer be marketed. The Final Rule marks the culmination of the agency's decision-making process, has the force of law, and was subject to the APA's notice and comment requirements, with which FDA complied."). The Final Rule, however, does not contain a substantive rule defining "unreasonable risk." Although the Final Rule is a substantive rule, the interpretation of "unreasonable risk" is not. Although Nutraceutical may not agree with FDA's interpretation of the "unreasonable risk" provision, that does not negate the fact that FDA was interpreting the statute, not making new law. Cf. Fertilizer Institute v. EPA, 935 F.2d 1303, 1308 (D.D.C. 1991) (noting that plaintiffs confused "the question whether the agency is interpreting a statute with the question whether the agency is thoroughly, or properly, interpreting the statute" when they argued that EPA's interpretation of a statutory provision was a legislative rule that should have been subject to notice-and-comment).

expert reviews. See 62 Fed. Reg. 30,678 (June 4, 1997); 62 Fed. Reg. 48,968 (Sept. 18, 1997); 65 Fed. Reg. 17,510 (Apr. 3, 2000); 65 Fed. Reg. 46,721 (July 31, 2000); 68 Fed. Reg. 10,417 (Mar. 5, 2003). From the 1997 Proposed Rule through the 2004 Final Rule, the rulemaking issues were the same - whether EDS were adulterated, and, if so, what to do about it. See Defs. Mem. at 4-6. Nutraceutical's argument that it did not foresee the consequences of the Final Rule (Pls. Opp. at 3) neither alters nor supplements the APA's notice and comment requirements. Indeed, Nutraceutical is trying to rewrite the APA by forcing FDA to define each word – i.e., “risk,” “benefit,” “comparison” – in its rule proposals. The APA does not require this.

Nutraceutical's claims that the Final Rule took the regulated industry by surprise because the adulteration standard "exceeded the widest breadth of the 1997 Proposed Rule" are baseless. Pls. Opp. at 4. In Nutraceutical's view, (i) the 1997 Proposed Rule defined "risk to exist at dose and serving levels where harm could be proven causally," whereas the Final Rule "defined a standard that did not require proof of causation,"⁴ and (ii) the 1997 Proposed Rule was limited to ephedrine alkaloids, whereas the Final Rule "create[s] a new adulteration standard for all dietary

⁴ Nutraceutical also rehashes its criticism of FDA's weighing of the evidence to determine that all EDS are adulterated. See Pls. Opp. at 7. This criticism is unwarranted. As FDA explained:

In evaluating whether dietary supplements containing ephedrine alkaloids present an unreasonable risk, we looked at the seriousness of the risks and the quality and persuasiveness of the totality of the evidence to support the presence of those risks. We then weighed the risks against the importance of the benefits and the quality and persuasiveness of the totality of the evidence to support the existence of those benefits.

69 Fed. Reg. at 6799. FDA thus evaluated the risks and benefits of EDS in a reasonable and evenhanded way, as the Tenth Circuit recognized. See Nutraceutical, 459 F.3d at 1043.

supplements."⁵ Both assertions, however, are unfounded. The purported departures from the 1997 Proposed Rule are chimeras manufactured by Nutraceutical, based on its mis-characterizations of FDA's explanations for its actions.⁶

Nutraceutical mistakenly concludes from FDA's discussion of adverse event reports in the 1997 Proposed Rule that the agency interpreted § 342(f)(1)(A) to require proof that EDS had caused harm.⁷ See Pls. Mem. at 2, 4. In fact, although FDA used adverse event reports as part of the evidence to support the proposed restrictions on EDS, FDA never intended to, and did not, increase its evidentiary burden beyond the showing of risk that the statute requires. The Proposed Rule never expressed the view that FDA was required – before taking action to protect the public health – to prove or show certainty of harm to any particular individual who consumed EDS. The Proposed Rule and the Final Rule both focused on *risk* of harm to the population of EDS consumers, not proof or certainty of harm to such consumers. See, e.g., 62 Fed. Reg. at

⁵ Nutraceutical also attempts to buttress its argument that the Final Rule was a radical departure from the 1997 Proposed Rule by repeatedly referring to the latter as an "enforcement action." See Pls. Opp. at 2, 4, 7-10. This is nothing but a mis-characterization, as the 1997 Proposed Rule was a notice of proposed rulemaking under 5 U.S.C. § 553(b), not an individual enforcement action.

⁶ Nutraceutical's continued insistence that FDA's use of the word "first" in the Final Rule was an admission that the agency was adopting a completely new regulatory approach is misplaced. Simply put, the 1997 Proposed Rule (and the Final Rule) represents the agency's first application of the *new provision added by DSHEA*. See Defs. Mem. at 14.

⁷ Nutraceutical's argument on this point is a thinly veiled attempt to take another crack at what it believes is FDA's lack of evidence to support the agency's determination that all EDS, regardless of dose, are adulterated because they present an unreasonable risk of illness or injury. Nutraceutical is not entitled at this stage of the case to impugn the evidence already accepted as "sufficiently probative" by the Tenth Circuit. Nutraceutical, 459 F.3d at 1043. Not only did the Tenth Circuit hold that the agency met its evidentiary burden, but also that FDA's rulemaking was entitled to the deferential arbitrary-and-capricious standard of review under the APA. Id. at 1038, 1043.

30,962 ("[I]t is apparent that there are serious and well-documented public health risks attendant to the use of ephedrine alkaloids in marketed dietary supplement products, and that the agency needs to propose actions to address these risks.").

Indeed, by its plain language, § 342(f)(1)(A) requires evidence of "significant or unreasonable risk" of illness or injury. FDA need not prove that a product has caused actual harm to a specific individual in a particular instance. Rather, FDA need only find that a product's *risk* of illness or injury to consumers outweighs its potential benefits in light of the claims and directions for use in the product's labeling or, if the labeling is silent, under ordinary conditions of use. If Congress had intended to require definitive proof that a dietary supplement "causes" harm, it would not have chosen the word "risk," and would have instead provided that a dietary supplement is adulterated if it "causes" illness or injury. See 69 Fed. Reg. at 6824.

Nutraceutical also claims that the Final Rule is impermissibly broader than the 1997 Proposed Rule because the proposed rule was limited to EDS whereas the Final Rule covers all dietary supplements. Pls. Opp. at 4, 8. This contention is wrong. Both the 1997 Proposed Rule ("Dietary Supplements Containing Ephedrine Alkaloids") and the Final Rule ("Final Rule Declaring Dietary Supplements Containing Ephedrine Alkaloids Adulterated Because They Present an Unreasonable Risk") declare or propose to declare that EDS, and not any other product, are adulterated.⁸ Compare 62 Fed. Reg. at 30,691 ("This proposal applies to dietary

⁸ Nutraceutical also claims, again, that there was an unexpected change between the adulteration standard in the 1997 Proposed Rule, which Nutraceutical calls the "Consolidated Standard," and the Final Rule, which applied the unreasonable risk standard. Because the hybrid standard Nutraceutical discerns in the 1997 Proposed Rule never existed, however, the alleged change never occurred. The fact that FDA used §§ 342(a)(1) and 342(f)(1)(A) in the same, or consecutive, sentence(s) in the 1997 Proposed Rule does not signify the creation of a hybridized statutory provision; rather, it signifies that FDA gave proper notice that it might rely on either or

supplements containing one or more ephedrine alkaloids") with 69 Fed. Reg. at 6793 ("This final rule applies to dietary supplements containing ephedrine alkaloids").

In any event, the agency's future application of the unreasonable risk standard to *other* dietary supplements is not before this Court. It is undisputed that Nutraceutical's product is an EDS product regulated by the Final Rule, and the FDA's application of § 342(f)(1)(A) to other types of dietary supplements is irrelevant.

II. THE FINAL RULE APPROPRIATELY DIFFERENTIATES BETWEEN DIETARY SUPPLEMENTS AND CONVENTIONAL FOODS

Nutraceutical is incorrect in arguing that "FDA's exemptions of ephedrine alkaloid containing foods and traditional Asian medicines (TAMs) from the 2004 Final Rule are arbitrary and capricious in violation of the APA." Pls. Opp. at 11. First, the Final Rule does not "exempt" ephedrine alkaloid-containing conventional foods or TAMs. Products cannot be exempted from a rule that could never have been applied to them in the first instance. As explained in the government's opening brief, as a matter of law, the Final Rule does not, and could not, apply to ephedrine alkaloid-containing conventional foods or products meeting the statutory definition of "drug" because these products cannot be found adulterated under the unreasonable risk provision of DSHEA, which applies only to dietary supplements and their dietary ingredients. See Defs. Mem. at 7-8.

Second, Nutraceutical's arguments in this regard seek to blur product distinctions created by the FDCA, particularly relating to the meaning of the statutory terms "food," "conventional food," "dietary supplement," and "dietary ingredient" and how they interrelate under the FDCA.

both of these provisions in the Final Rule. See Defs. Mem. at 11-13.

After correctly pointing out that dietary supplements are deemed to be foods under the FDCA, Nutraceutical then draws the erroneous conclusion that therefore all dietary supplement adulteration provisions of the FDCA, including the "unreasonable risk" provision, must apply to all types of food, including conventional foods, such as tea. See Pls. Opp. at 11-12. In addition to the obvious logical fallacy in this reasoning, Nutraceutical ignores the fact that "food" and "conventional food" each has a distinct meaning under the FDCA.

Although it is true that the FDCA generally deems dietary supplements to be foods, it is *not* true that dietary supplements are deemed to be *conventional* foods. Rather, dietary supplements and conventional foods are mutually exclusive subcategories of the larger category of foods to which they both belong. See 21 U.S.C. § 321(f) (defining "food"); 21 U.S.C. § 321(ff)(2)(B)-(C) (defining dietary supplements and conventional foods as mutually exclusive based on how they are labeled and represented).

These distinctions are important under the FDCA's statutory scheme. Some adulteration provisions of the FDCA apply to all foods, including dietary supplements and dietary ingredients.⁹ See, e.g., 21 U.S.C. § 342(a)(1), 342(a)(3) (foods that consist in whole or in part of a "filthy, putrid, or decomposed substance" or that are "otherwise unfit for food" are adulterated). Others apply only to conventional foods. See, e.g., 21 U.S.C. § 342(e) (adulteration provision specific to butter and margarine), 342(d)(1)-(3) (adulteration provisions specific to candy and

⁹ "Dietary ingredient" is defined by enumeration in the FDCA's dietary supplement definition, added by DSHEA. See 21 U.S.C. § 321(ff)(1). The term "dietary ingredient" did not appear in the FDCA before DSHEA and is used exclusively to refer to substances intended for use as or in dietary supplements (e.g., vitamins, minerals, amino acids). Contrary to Nutraceutical's suggestion (Pls. Opp. at 11), the FDCA does not use the term "dietary ingredient" to refer to ingredients of conventional foods.

other confectioneries). Still others, like § 342(f)(1)(A) and the other subparagraphs of § 342(f)(1), by their plain terms apply only to dietary supplements and dietary ingredients. See 21 U.S.C. § 342(f)(1) (A food is adulterated if it "*is a dietary supplement or contains a dietary ingredient* that" (emphasis added)). Nutraceutical's contentions aside, Congress drew the regulatory distinctions between dietary supplements and conventional foods in the plain language of DSHEA.

Finally, Nutraceutical's contention that "a complete ban on foods containing ephedrine alkaloids in the Final Rule would have been rational" is self-defeating and irrelevant. See Pls. Opp. at 13. Because the 1997 Proposed Rule did not propose any restrictions on conventional foods containing ephedrine alkaloids (see 62 Fed. Reg. at 30,691), a Final Rule that banned such products (in addition to EDS) would have been a "startlingly complete substantive break" (Pls. Mem. at 11) from the 1997 Proposed Rule. Moreover, Nutraceutical has no authority to dictate the scope, manner, or timing of FDA's regulatory activities. FDA has the discretion to determine its regulatory priorities in furtherance of its mission to protect the public health.

CONCLUSION

For the foregoing reasons, this Court should deny Plaintiffs' Motion for Summary Judgment and grant Defendants' Cross-Motion for Summary Judgment.

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on this 21st day of February, 2007, I electronically filed a true and correct copy of “DEFENDANTS' REPLY TO PLAINTIFFS' OPPOSITION TO DEFENDANTS' CROSS-MOTION FOR SUMMARY JUDGMENT” with the Clerk of the Court using the CM/ECF system which is relied upon to then promptly send notification of filing electronically with a copy of the filing to at least the following e-filers:

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